Remarks

Claims 1-2, 8-18, 60, 64-65, 75 and 78-80 are in condition for allowance according to the Office Action dated January 26, 2005. Claims 77 and 81 have been rejected. Subsequent to the entry of the present amendment, claims 1, 2, 8-18, 60, 64-65, 75, 77-81 are pending and at issue. No new matter has been added. The pending claims are fully supported by the specification and original claims.

The Rejection under 35 U.S.C. § 112, First Paragraph, Enablement

Claims 77 and 81 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly not enabled by the specification as filed. Applicant respectfully traverses the rejection as it may apply to the pending claims.

At page 2, part 4, the Office Action states that the specification is only enabling for, in part, a method of localizing a probe within a cell using a single chain antibody comprising "the amino acid sequence set forth in SEQ ID NO:2 or an amino acid sequence encoded by the nucleic acid sequence set forth in SEQ ID NO:1." Applicant notes that allowed claims 1 and 60 are not limited to a single chain antibody having a particular amino acid sequence. The antibodies suitable for use in the claimed methods are limited only to those that specifically bind to the fully-characterized antigen 4-ethoxymethylene-2-phenyl-2-oxazolin-5-one (i.e., phOx). Despite the fact that the present claims do not claim an isolated antibody, case law and Office guidelines promulgated for examination of such antibody claims under section 112, paragraph 1, are instructive and relevant to the present discussion.

Briefly, the courts have consistently held that as long as an applicant has disclosed a "fully characterized antigen, either by its structure, formula, chemical name, or physical properties, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen." Noelle, 355 F.3d at 1349 (Fed. Cir. 2004). In addition, the Office appears to have taken the position that a claim directed to any antibody which is capable of binding to antigen X' would have sufficient support in a written

description that disclosed fully characterized antigens (see page 60 of "Synopsis of Application of Written Description Guidelines" available at http://www.uspto.gov/web/menu/written.pdf).

The single chain antibodies recited in claims 1 and 60 specifically bind to the fully-characterized antigen 4-ethoxymethylene-2-phenyl-2-oxazolin-5-one (i.e., phOx). According to current case law and Office guidelines, it is unnecessary for these antibodies to be further defined by particular amino acid sequences in order to satisfy section 112, paragraph 1.

In addition, U.S. Patent No. 6,017,754 ('754 patent) was cited in a § 103 rejection set forth in part 7 of the Office Action dated April 22, 2003. The issued claims recite an expression vector comprising a DNA sequence encoding a single chain antibody. Claim 1 of the '754 patent reads in part:

> 1. A eukaryotic expression vector ... comprising:
> a first DNA sequence encoding an anti-hapten single-chain antibody, which antibody binds to a specific hapten, wherein said hapten is 4-ethoxymethylene-2-phenyl-2-oxazolin-5-one (i.e., phOx).[1]

The antibodies recited in exemplary claim 1 of the '754 patent are clearly defined by the fully-characterized antigen (i.e., phOx) to which they bind. These antibodies are defined in a manner consistent with prevailing case law and Office guidelines. As noted above, the phOx hapten also defines the antibodies recited in claims 1 and 60 of the instant application which is similarly consistent with the case law and guidelines discussed above. Accordingly, Applicant maintains that the allowed claims 1 and 60 are not limited to a single chain antibody having a particular amino acid sequence.

With regard to claims 77 and 81 the Examiner has taken the position that, while the specification is enabling for an isolated nucleic acid comprising a polynucleotide encoding

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[1] U.S. Patent No. 6,017,754, column 33, lines 40-44.

SEQ ID NO:2 and a polynucleotide comprising SEQ ID NO:1, the specification does not reasonably provide enablement for: 1) the amino acid sequence set forth in SEQ ID NO:2 with up to 30 conservative amino acid substitutions; 2) an amino acid sequence at least 95% identical to SEQ ID NO:2; or 3) an amino acid sequence encoded by a nucleic acid sequence at least 95% identical to SEQ ID NO:1.

An analysis of whether the claims under examination are supported by an enabling disclosure requires a determination of whether that disclosure contains sufficient information regarding the subject matter of the examined claims as to enable one skilled in the pertinent art to make and use the claimed invention. In order to establish a prima facie case of lack of enablement, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. In the present case the Examiner has provided an analysis of several of the relevant enablement factors on pages 2-6 of the Office Action. One of the Examiner's primary arguments is that the specification only discloses one single chain antibody that binds specifically to phOx. The Examiner also argues that the specification does not disclose any working example demonstrating that any modification to SEQ ID NO:2 still binds to phOx for the claimed method. The Examiner relies on Skolnick, Ngo, Abaza and Winkler to support the position that even single amino acid substitutions in single chain antibody can exert drastic effects on the binding specificity of the antibody (see Office Action at page 4).

The examiner concludes (see page 4):

> Given the lack of guidance as to which specific nucleotide within SEQ ID NO:1, the corresponding amino acid residues within the full length sequence of SEQ ID NO:2 can be substituted, deleted, and combination thereof, it is unpredictable which single chain antibody comprising an undisclosed polypeptide with no more than 30 amino acid substitutions encoded by the undisclosed polynucleotide would maintain its binding specificity to phOx, in turn, useful for the claimed method.

Applicant notes that amended claim 77 and new claim 81 depend from independent claims 1 and 60, respectively. Thus, claims 77 and 81 contain all of the limitations set forth in method claims 1 and 60. Since the independent claims have been deemed allowable, then any

claim which depends therefrom should similarly be allowable. As noted above, Applicant has defined the single chain antibody of claims 1 and 60 in a manner consistent with prevailing case law and Office guidelines, i.e., the single chain antibody is defined by its ability to bind specifically to the fully-characterized antigen phOx. Claims 77 and 81 merely further define the antibody as having particular amino acid sequences encoded by particular nucleic acid sequences. It is Applicants position that the Examiner has failed to establish that the instant disclosure is not enabling for single chain antibodies defined by their ability to bind specifically to the fully-characterized antigen phOx. By extension, the Examiner has similarly failed to establish that the instant disclosure is not enabling for single chain antibodies defined by their ability to bind to the phOx antigen *and* possess amino acid sequences as defined in claims 77 or 81.

Applicant submits that, upon reading the disclosure, those of ordinary skill in the art would have been provided a reasonable amount of guidance to make and use single chain antibodies defined by their ability to bind to the phOx antigen *and* possess amino acid sequences as defined in claims 77 or 81. Accordingly, Applicant requests withdrawal of the rejection of claims 77 and 81 under 35 U.S.C. § 112, first paragraph.

The Rejection under 35 U.S.C. § 112, First Paragraph, Written Description

Claims 77 and 81 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly not adequately described by the specification. Applicant respectfully traverses the rejection as it may apply to the pending claims.

Applicant disagrees with the Examiner that claims 77 and 81 lack written description in the specification and that Applicants were not in possession of the claimed invention at the time the application was filed simply because "the specification discloses only one single chain antibody that binds to phOx" (see Office Action at page 6, part 5, paragraph 3). First, with regard to the pending claims generally, the examination guidelines for examination of claims directed to antibodies indicate that any antibody which is capable of binding to antigen X' would have sufficient support in a written description that disclosed fully characterized

antigens (see page 60 of "Synopsis of Application of Written Description Guidelines" available at http://www.uspto.gov/web/menu/written.pdf).

Second, with regard to claims 77 and 81 specifically, to satisfy the written description requirement it is not necessary that the application describe the claim limitations exactly, but only so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that appellants invented the claimed subject matter. The Enzo court stated that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316 at 1324. In addition, the court in Noelle noted that "[T]he PTO would find compliance with 112, paragraph 1, for a claim to an isolated antibody capable of binding to antigen X, notwithstanding the functional definition of the antibody, in light of the well defined structural characteristics for the five classes of antibody, the functional characteristics of antibody binding, and the fact that the antibody technology is well developed and mature" (355 F.3d at 1349 (Fed. Cir. 2004) (quoting Enzo BioChem, Inc. v. Gen-Probe, Inc., 323 F.3d 956, 964 (Fed. Cir. 2002)).

The present specification specifically describes the chemical structures of a polynucleotide that encodes a polypeptide of SEQ ID NO:2 and a polynucleotide comprising the coding sequence set forth in SEQ ID NO:1. The specification also provides the fully-characterized antigen 4-ethoxymethylene-2-phenyl-2-oxazolin-5-one (phOx) to which the single chain antibody binds. Contrary to the examiner's position, it would reasonably appear that such a description in the specification would constitute sufficiently detailed, relevant identifying characteristics of the claimed subject matter consistent with Enzo (supra). Applicant submits that the examiner has failed to indicate why one of ordinary skill in the art, who is in possession of the very specific chemical structures set forth in SEQ ID NOs:1 and 2, and a fully characterized antigen such as PhOx, would be unable to recognize, upon reading

the disclosure, that Applicants were not in possession of the single chain antibodies set forth in the claimed methods.

Those of ordinary skill in the art would have recognized from reading the disclosure that the inventors had invented methods that utilize single chain antibodies that bind to phOx. The skilled artisan would also recognize that the antibodies could be further defined by specific nucleotide and amino acid sequences and variations of these sequences. These teachings clearly indicate that the present inventors were in possession of the methods as claimed, at the time of filing of the patent application. Accordingly, Applicant requests withdrawal of the rejection of the claims under 35 U.S.C. § 112, first paragraph as allegedly not adequately described by the specification as filed.

Claims 77 and 81 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly not adequately described by the specification. This rejection is a new matter rejection. Applicant respectfully traverses the rejection as it may apply to the pending claims.

Specifically, the Office Action alleges that "the passages pointed out by the applicant in the amendment filed 10/28/04 do not provide clear support" for the following phrases: 1) SEQ ID NO:2 with up to 30 conservative amino acid substitutions; 2) at least 95% identical to SEQ ID NO:2; and 3) a nucleic acid sequence at least 95% identical to SEQ ID NO:1.

In the response filed October 28, 2004 Applicant indicated that support for claims 77 and 81 could be found beginning at page 11, line 11, bridging to page 13, line 23. If the Examiner is seeking the express or explicit disclosure of all elements of claims 77 or 81, then such "clear support" is clearly lacking from the aforementioned passages. However, it is Applicant's understanding that claimed subject matter need not be described in haec verba to satisfy the description requirement. It is Applicant's further understanding that the application need only describe the claim limitations "so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that appellants invented processes including those limitations" (See, e.g., In re Herschler, 591 F.2d 693, 700 (CCPA 1979)). Accordingly, Applicants review of pages 11-13 of the pending application indicates that the information

contained therein clearly meets the written description requirements of section 112, first paragraph, as interpreted by the courts.

For example, the recitation of "conservative amino acid substitutions" in claims 77 and 81 is clearly supported by the specification at page 13, lines 12-24. This passage describes the "interchangeability of residues" (at line 14) in an amino acid sequence of a polypeptide when the changes entail the use of conservative residues. The specification need not recite "up to 30" conservative amino acid substitutions in order for the skilled artisan to clearly recognize that such substitutions could made in the polypeptide set forth in SEQ ID NO:2 and that a polypeptide so modified could still bind to phOx. Similarly, the specification need not specifically recite "at least 95% identical to SEQ ID NO:2" or "a nucleic acid sequence at least 95% identical to SEQ ID NO:1" in order for the skilled artisan to recognize that the disclosure at pages 11 and 12 supports those limitations as they appear in Applicant's claimed method.

Accordingly, Applicant requests withdrawal of the rejection of the claims under 35 U.S.C. § 112, first paragraph as allegedly not adequately described by the specification as filed.

In view of the above remarks, reconsideration and favorable action on all claims is respectfully requested. Should any questions remain in view of this communication, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved. Please charge any additional fees, or make any credits, to Deposit Account No. 07-1896.

Respectfully submitted,

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